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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/818,260	03/26/2001	Nicholas J. Schork	GENSET.076C1	9223
23557	7590	12/03/2003	EXAMINER	
SALIWANCHIK LLOYD & SALIWANCHIK A PROFESSIONAL ASSOCIATION 2421 N.W. 41ST STREET SUITE A-1 GAINESVILLE, FL 326066669			KENEDY, ANDREW A	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 12/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/818,260	SCHORK ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Andrew A. Kenedy	1631	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) 10-39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) 1-39 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 May 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All   b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____.  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                    | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election without traverse of Group I (claims 1-9) in the response filed October 29, 2003, is acknowledged.

Claims 10-39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the response filed October 29, 2003.

### ***Specification***

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) and 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

In the reference claiming priority to the provisional application bearing the filing date of July 28, 2000, applicant has omitted the application No.

Applicant has failed to include a reference claiming benefit to nonprovisional application No. 09/635502, filed August 9, 2000, priority to which was claimed in the transmittal document of March 26, 2001, and the oath.

***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The method of claims 1-3 is a purely mathematical and theoretical exercise resulting in the manipulation of data. Specifically, the method is a mathematical exercise in statistical computation that does not produce a useful, concrete, and tangible result.

The system of claims 4-6 is non-statutory because the "system", as claimed, can be viewed simply as data. For example, a piece of paper with written instructions for the method, or a non-computer-executable text file with instructions for the method are both just data, but are also each a "system" for executing the method.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-3, 5-6, and 8-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4, and 7 require the goal of determining the statistical significance of a difference between haplotype frequency profiles of at least two groups of individuals, the final

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method step of these three claims being to determine the significance of this difference by simulating hypothetical groups by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes. However, claims 2, 5, and 8 are confusing because they require the generation of information -- the calculation of all possible single-haplotype chi-square tests prior to determining the significance of the difference between likelihoods -- that is not used in the final or any other method step of claims 1, 4, and 7. If this information is supposed to be used, then it is unclear how it is to be used since the instant claims do not specify how. Likewise, claims 3, 6, and 9 require the generation of information -- assessing the statistical significance of individual haplotypes using an odds ratio or a P-excess value -- that is not used in the final or any other method step of claims 1, 4, and 7. If this information is supposed to be used, then it is unclear how it is to be used since the instant claims do not specify how.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stanton, Jr. (US 2002/0039990 A1) in view of Blumenfeld et al. (US 6528260 B1).

Applicant is accorded benefit to provisional application No. 60/207904 with a priority date of May 25, 2000, for the claims.

The disclosure of Stanton, Jr., relied upon in this rejection, receives benefit to at least the filing date of July 20, 1999, of parent application No. 09/357743. As such, Stanton, Jr. is valid prior art under 103(a) against the instant claims. The disclosure of Blumenfeld et al., also relied upon in this rejection, receives benefit to at least the filing date of March 25, 1999, of provisional application No. 60/126269. As such, Blumenfeld et al. is valid prior art under 103(a) against the instant claims.

Stanton, Jr. teaches a method of determining the statistical significance of a difference between haplotype frequency profiles of at least two groups of individuals comprising: determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes, determining the sum of the separate likelihoods that each of said at least two groups of individuals are derived from the same distribution of haplotypes, and determining the difference of said sum and said combined likelihood (see at least page 65, paragraph [0825]).

Stanton, Jr. teaches the use of permutation tests for statistical analysis (pg. 38, paragraphs [0414], [0415], and [0418]; and pg. 40-41, paragraph [0467]), but does not specifically teach randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes. Stanton, Jr. teaches the use of a chi-square test in determining the significance of the difference between said sum and said combined likelihood (pg. 65, paragraph [0825]), but does not specifically teach calculating all possible single-haplotype chi-square tests. Stanton, Jr. teaches the use of an odds ratio in statistical hypothesis testing (see at least pg. 38, paragraphs [0417] and [0418]), but does not teach

assessing the statistical significance of individual haplotypes using an odds ratio or a P-excess value.

Blumenfeld et al. teaches determining the statistical significance of a haplotype analysis by simulating hypothetical groups, by randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes (col. 90, lines 27-42); calculating all possible single-haplotype chi-square tests (col. 89, line 62 through col. 90, line 6); and assessing the statistical significance of individual haplotypes using an odds ratio (col. 90, line 51 through col. 91, line 11).

It would have been obvious for one of ordinary skill in the art to incorporate the random permutation of haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes as taught by Blumenfeld et al., into the method of Stanton, Jr., since Blumenfeld et al. teaches that phenotype permutation tests are used "to confirm the statistical significance of first stage haplotype analysis" (col. 90, lines 28-29). It would have been obvious for one of ordinary skill in the art to incorporate the calculation of all possible single-haplotype chi-square tests as taught by Blumenfeld et al., into the method of Stanton, Jr., since Blumenfeld et al. teaches that calculation of single-haplotype chi-square tests will "determine if there is a statistically significant correlation between the haplotype and the phenotype (trait) under study" (col. 89, lines 65-67). It would have been obvious for one of ordinary skill in the art to incorporate the assessment of the statistical significance of individual haplotypes using an odds ratio as taught by Blumenfeld et al., into the method of Stanton, Jr., since Blumenfeld et al. teaches that assessing the statistical significance of individual haplotypes using an odds ratio is used to determine if there is "the association between a risk factor (in

genetic epidemiology the risk factor is the presence or the absence of a certain allele or haplotype at marker loci) and a disease" (col. 90, lines 52-55).

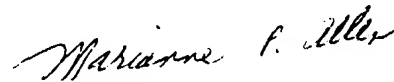
Since the method of both Stanton, Jr. and Blumenfeld et al. are implemented using computer systems (see at least pg. 65, paragraph [0825], lines 8-15 of Stanton, Jr.; and at least col. 117, line 66 through col. 118, line 2 of Blumenfeld et al.), the system of claims 4-6 and the programmed storage device of claims 7-9 are obvious for the same reasons.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew A. Kenedy whose telephone number is 703-305-4842. The examiner can normally be reached on Monday-Friday 9:00am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 703-308-4028. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-305-4842.

AAK  
November 25, 2003

  
MARIANNE P. ALLEN  
PRIMARY EXAMINER  
GROUP 1800  
Ac1631